

SEQUENCE LISTING

<110> De Francesco, Raffaele
Tomei, Licia
Behrens, Sven-Erik

<120> METHOD FOR REPRODUCING IN VITRO THE
RNA-DEPENDENT RNA POLYMERASE AND TERMINAL NUCLEOTIDYL
TRANSFERASE ACTIVITIES ENCODED BY HEPATITIS C VIRUS (HCV)

<130> IT0002PCA

<150> 08/952,981

<151> 1998-03-23

<150> PCT/IT96/00106

<151> 1996-05-24

<150> RM95A000343

<151> 1995-05-25

<160> 14

<170> FastSEQ for Windows Version 4.0

<210> 1

<211> 591

<212> PRT

<213> Hepatitis C virus

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His	His	Asn	Met	Val	Tyr	Ala	Thr	Ser	Arg	Ser	Ala	Gly	Leu	Arg	
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Gln	Lys	Lys	Val	Thr	Phe	Asp	Arg	Leu	Gln	Val	Leu	Asp	Asp	His	Tyr
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Lys	Leu	Leu	Ser	Val	Glu	Glu	Ala	Cys	Lys	Leu	Thr	Pro	Pro	His	Ser
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Val	Phe	Pro	Asp	Leu	Gly	Val	Arg	Val	Cys	Glu	Lys	Met	Ala	Leu	Tyr
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Gln Cys Cys Asp Leu Ala Pro Glu Ala Arg Gln Ala Ile Lys Ser Leu
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Thr Glu Arg Leu Tyr Ile Gly Gly Pro Leu Thr Asn Ser Lys Gly Gln
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Asn Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Thr Thr Ser
      275      280      285
Cys Gly Asn Thr Leu Thr Cys Tyr Leu Lys Ala Ser Ala Ala Cys Arg
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Ala Ala Lys Leu Gln Asp Cys Thr Met Leu Val Asn Gly Asp Asp Leu
      305      310      315      320
Val Val Ile Cys Glu Ser Ala Gly Thr Gln Glu Asp Ala Ala Ser Leu
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Arg Val Phe Thr Glu Ala Met Thr Arg Tyr Ser Ala Pro Pro Gly Asp
      340      345      350
Pro Pro Gln Pro Glu Tyr Asp Leu Glu Leu Ile Thr Ser Cys Ser Ser
      355      360      365
Asn Val Ser Val Ala His Asp Ala Ser Gly Lys Arg Val Tyr Tyr Leu
      370      375      380
Thr Arg Asp Pro Thr Thr Pro Leu Ala Arg Ala Ala Trp Glu Thr Ala
      385      390      395      400
Arg His Thr Pro Val Asn Ser Trp Leu Gly Asn Ile Ile Met Tyr Ala
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Pro Thr Leu Trp Ala Arg Met Ile Leu Met Thr His Phe Phe Ser Ile
      420      425      430
Leu Leu Ala Gln Glu Gln Leu Glu Lys Ala Leu Asp Cys Gln Ile Tyr
      435      440      445
Gly Ala Cys Tyr Ser Ile Glu Pro Leu Asp Leu Pro Gln Ile Ile Glu
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Arg Leu His Gly Leu Ser Ala Phe Ser Leu His Ser Tyr Ser Pro Gly
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Glu Ile Asn Arg Val Ala Ser Cys Leu Arg Lys Leu Gly Val Pro Pro
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Leu Arg Val Trp Arg His Arg Ala Arg Ser Val Arg Ala Arg Leu Leu
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Ala Val Lys Thr Lys Leu Lys Leu Thr Pro Ile Pro Ala Ala Ser Arg
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Tyr His Ser Leu Ser Arg Ala Arg Pro Arg Trp Phe Met Leu Cys Leu
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His Val Trp Ile Pro Pro Leu Asn Ala Arg Gly Gly Arg Asp Ala Ile
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Cys	Met	Leu	Val	Arg	Lys	Val	Ala	Gly	Gly	His	Tyr	Val	Gln	Met	Ala
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Ala	Val	Glu	Pro	Val	Val	Phe	Ser	Asp	Met	Glu	Thr	Lys	Ile	Ile	Thr
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Gly	Asp	Ser	Arg	Gly	Ser	Leu	Leu	Ser	Pro	Arg	Pro	Val	Ser	Tyr	Leu
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Gly Gly Pro Leu Thr Asn Ser Lys Gly Gln Asn Cys Gly Tyr Arg Arg
1875 1880 1885
Cys Arg Ala Ser Gly Val Leu Thr Thr Ser Cys Gly Asn Thr Leu Thr
1890 1895 1900
Cys Tyr Leu Lys Ala Ser Ala Ala Cys Arg Ala Ala Lys Leu Gln Asp
1905 1910 1915 1920
Cys Thr Met Leu Val Asn Gly Asp Asp Leu Val Val Ile Cys Glu Ser
1925 1930 1935
Ala Gly Thr Gln Glu Asp Ala Ala Ser Leu Arg Val Phe Thr Glu Ala
1940 1945 1950
Met Thr Arg Tyr Ser Ala Pro Pro Gly Asp Pro Pro Gln Pro Glu Tyr
1955 1960 1965
Asp Leu Glu Leu Ile Thr Ser Cys Ser Ser Asn Val Ser Val Ala His
1970 1975 1980
Asp Ala Ser Gly Lys Arg Val Tyr Tyr Leu Thr Arg Asp Pro Thr Thr
1985 1990 1995 2000
Pro Leu Ala Arg Ala Ala Trp Glu Thr Ala Arg His Thr Pro Val Asn
2005 2010 2015
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2020 2025 2030
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2050 2055 2060

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gcccugcagg cugaaaagcu ggaccaccau cccgaguggu uuaacgugua caacaagguc 300
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SEQUENCE LISTING

GENERAL INFORMATION

- (i) APPLICANT: ISTITUTO DI RICERCHE DI BIOLOGIA
MOLECOLARE P. ANGELETTI S.p.A.
- 5 (ii) TITLE OF INVENTION: METHOD FOR REPRODUCING
IN VITRO THE RNA-DEPENDENT RNA POLYMERASE
AND TERMINAL NUCLEOTIDYL TRANSFERASE
ACTIVITIES ENCODED BY HEPATITIS C VIRUS
(HCV)
- 10 (iii) NUMBER OF SEQUENCES: 14
- (iv) CORRESPONDENCE ADDRESS:
(A)ADDRESSEE: Societa Italiana Brevetti
(B)STREET: Piazza di Pietra, 39
(C)CITY: Rome
- 15 (D)COUNTRY: Italy
(E)POSTAL CODE: 1-00186
- (v) COMPUTER READABLE FORM:
(A)MEDIUM TYPE: Floppy disk 3.5" 1.44
MBYTES
- 20 (B)COMPUTER: IBM PC compatible
(C)OPERATING SYSTEM: PC-DOS/MS-DOS Rev.6.22
(D)SOFTWARE: Microsoft Word 6.0
- (viii) ATTORNEY INFORMATION
(A)NAME: DI CERBO, Mario (Dr.)
- 25 (C)REFERENCE: RM/X88530/PCT-DC
- (ix) TELECOMMUNICATION INFORMATION
(A)TELEPHONE: 06/6785941
(B)TELEFAX: 06/6794692
(C)TELEX: 612287 ROPAT
- 30 (1) INFORMATION FOR SEQ ID NO: 1:
- (i) SEQUENCE CHARACTERISTICS
(A)LENGTH: 591 amino acids
(B)TYPE: amino acid
- 35 (C)STRANDEDNESS: single
(D)TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein

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- (iii) HYPOTHETICAL: No
 (iv) ANTISENSE: No
 (v) FRAGMENT TYPE: C-terminal fragment
 (vi) ORIGINAL SOURCE:
 5 (A) ORGANISM: Hepatitis C Virus
 (C) ISOLATE : BK
 (vii) IMMEDIATE SOURCE: cDNA clone pCD(38-9.4)
 described by Tomei et al. 1993
 (ix) FEATURE:
 10 (A) NAME: NS5B Non-structural polyprotein
 (C) IDENTIFICATION METHOD: Experimentally
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:
- | | | | | | | | | | | | | | | | | | | | | |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | Ser | Met | Ser | Tyr | Thr | Trp | Thr | Gly | Ala | Leu | Ile | Thr | Pro | Cys | Ala | Ala | 1 | 5 | 10 | 15 |
| 15 | Glu | Glu | Ser | Lys | Leu | Pro | Ile | Asn | Ala | Leu | Ser | Asn | Ser | Leu | Leu | Arg | 20 | 25 | 30 | |
| | His | His | Asn | Met | Val | Tyr | Ala | Thr | Thr | Ser | Arg | Ser | Ala | Gly | Leu | Arg | 35 | 40 | 45 | |
| 20 | Gln | Lys | Lys | Val | Thr | Phe | Asp | Arg | Leu | Gln | Val | Leu | Asp | Asp | His | Tyr | 50 | 55 | 60 | |
| | Arg | Asp | Val | Leu | Lys | Glu | Met | Lys | Ala | Lys | Ala | Ser | Thr | Val | Lys | Ala | 65 | 70 | 75 | 80 |
| | Lys | Leu | Leu | Ser | Val | Glu | Glu | Ala | Cys | Lys | Leu | Thr | Pro | Pro | His | Ser | 85 | 90 | 95 | |
| 25 | Ala | Lys | Ser | Lys | Phe | Gly | Tyr | Gly | Ala | Lys | Asp | Val | Arg | Asn | Leu | Ser | 100 | 105 | 110 | |
| | Ser | Lys | Ala | Val | Asn | His | Ile | His | Ser | Val | Trp | Lys | Asp | Leu | Leu | Glu | 115 | 120 | 125 | |
| 30 | Asp | Thr | Val | Thr | Pro | Ile | Asp | Thr | Thr | Ile | Met | Ala | Lys | Asn | Glu | Val | 130 | 135 | 140 | |
| | Phe | Cys | Val | Gln | Pro | Glu | Lys | Gly | Gly | Arg | Lys | Pro | Ala | Arg | Leu | Ile | 145 | 150 | 155 | 160 |
| | Val | Phe | Pro | Asp | Leu | Gly | Val | Arg | Val | Cys | Glu | Lys | Met | Ala | Leu | Tyr | 165 | 170 | 175 | |
| 35 | Asp | Val | Val | Ser | Thr | Leu | Pro | Gln | Val | Val | Met | Gly | Ser | Ser | Tyr | Gly | 180 | 185 | 190 | |
| | Phe | Gln | Tyr | Ser | Pro | Gly | Gln | Arg | Val | Glu | Phe | Leu | Val | Asn | Thr | Trp | | | | |

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	195	200	205
	Lys Ser Lys Lys Asn Pro Met Gly Phe Ser Tyr Asp Thr Arg Cys Phe		
	210	215	220
5	Asp Ser Thr Val Thr Glu Asn Asp Ile Arg Val Glu Glu Ser Ile Tyr		
	225	230	235 240
	Gln Cys Cys Asp Leu Ala Pro Glu Ala Arg Gln Ala Ile Lys Ser Leu		
	245	250	255
	Thr Glu Arg Leu Tyr Ile Gly Gly Pro Leu Thr Asn Ser Lys Gly Gln		
10	260	265	270
	Asn Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Thr Thr Ser		
	275	280	285
	Cys Gly Asn Thr Leu Thr Cys Tyr Leu Lys Ala Ser Ala Ala Cys Arg		
	290	295	300
15	Ala Ala Lys Leu Gln Asp Cys Thr Met Leu Val Asn Gly Asp Asp Leu		
	305	310	315 320
	Val Val Ile Cys Glu Ser Ala Gly Thr Gln Glu Asp Ala Ala Ser Leu		
	325	330	335
	Arg Val Phe Thr Glu Ala Met Thr Arg Tyr Ser Ala Pro Pro Gly Asp		
20	340	345	350
	Pro Pro Gln Pro Glu Tyr Asp Leu Glu Leu Ile Thr Ser Cys Ser Ser		
	355	360	365
	Asn Val Ser Val Ala His Asp Ala Ser Gly Lys Arg Val Tyr Tyr Leu		
	370	375	380
25	Thr Arg Asp Pro Thr Thr Pro Leu Ala Arg Ala Ala Trp Glu Thr Ala		
	385	390	395 400
	Arg His Thr Pro Val Asn Ser Trp Leu Gly Asn Ile Ile Met Tyr Ala		
	405	410	415
	Pro Thr Leu Trp Ala Arg Met Ile Leu Met Thr His Phe Phe Ser Ile		
30	420	425	430
	Leu Leu Ala Gln Glu Gln Leu Glu Lys Ala Leu Asp Cys Gln Ile Tyr		
	435	440	445
	Gly Ala Cys Tyr Ser Ile Glu Pro Leu Asp Leu Pro Gln Ile Ile Glu		
	450	455	460
35	Arg Leu His Gly Leu Ser Ala Phe Ser Leu His Ser Tyr Ser Pro Gly		
	465	470	475 480
	Glu Ile Asn Arg Val Ala Ser Cys Leu Arg Lys Leu Gly Val Pro Pro		

15

(2) INFORMATION FOR SEQ ID NO: 2:

(i) SEQUENCE CHARACTERISTICS

(A) LENGTH: 2201 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: polypeptide

(iii) HYPOTHETICAL: No

(iv) ANTISENSE: No

(v) FRAGMENT TYPE: C-terminal fragment

(vii) IMMEDIATE SOURCE: cDNA clone pCD(38-9.4)

described by Tomei et al. 1993

(ix) FEATURE:

(A) NAME: NS2-NS5B Nonstructural Protein

Precursor

(C) IDENTIFICATION METHOD: Experimentally

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

Met Asp Arg Glu Met Ala Ala Ser Cys Gly Gly Ala Val Phe Val Gly
1 5 10 15

35 Leu Val Leu Leu Thr Leu Ser Pro Tyr Tyr Lys Val Phe Leu Ala Arg
 20 25 30

Leu Ile Trp Trp Leu Gln Tyr Phe Thr Thr Arg Ala Glu Ala Asp Leu

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	35	40	45
	His Val Trp Ile Pro Pro Leu Asn Ala Arg Gly Gly Arg Asp Ala Ile		
	50	55	60
	Ile Leu Leu Met Cys Ala Val His Pro Glu Leu Ile Phe Asp Ile Thr		
5	65	70	75
	Lys Leu Leu Ile Ala Ile Leu Gly Pro Leu Met Val Leu Gln Ala Gly		
	85	90	95
	Ile Thr Arg Val Pro Tyr Phe Val Arg Ala Gln Gly Leu Ile His Ala		
	100	105	110
10	Cys Met Leu Val Arg Lys Val Ala Gly Gly His Tyr Val Gln Met Ala		
	115	120	125
	Phe Met Lys Leu Gly Ala Leu Thr Gly Thr Tyr Ile Tyr Asn His Leu		
	130	135	140
	Thr Pro Leu Arg Asp Trp Pro Arg Ala Gly Leu Arg Asp Leu Ala Val		
15	145	150	155
	Ala Val Glu Pro Val Val Phe Ser Asp Met Glu Thr Lys Ile Ile Thr		
	165	170	175
	Trp Gly Ala Asp Thr Ala Ala Cys Gly Asp Ile Ile Leu Gly Leu Pro		
	180	185	190
20	Val Ser Ala Arg Arg Gly Lys Glu Ile Leu Leu Gly Pro Ala Asp Ser		
	195	200	205
	Leu Glu Gly Arg Gly Leu Arg Leu Leu Ala Pro Ile Thr Ala Tyr Ser		
	210	215	220
	Gln Gln Thr Arg Gly Leu Leu Gly Cys Ile Ile Thr Ser Leu Thr Gly		
25	225	230	235
	Arg Asp Lys Asn Gln Val Glu Gly Glu Val Gln Val Val Ser Thr Ala		
	245	250	255
	Thr Gln Ser Phe Leu Ala Thr Cys Val Asn Gly Val Cys Trp Thr Val		
	260	265	270
30	Tyr His Gly Ala Gly Ser Lys Thr Leu Ala Ala Pro Lys Gly Pro Ile		
	275	280	285
	Thr Gln Met Tyr Thr Asn Val Asp Gln Asp Leu Val Gly Trp Pro Lys		
	290	295	300
	Pro Pro Gly Ala Arg Ser Leu Thr Pro Cys Thr Cys Gly Ser Ser Asp		
35	305	310	315
	Leu Tyr Leu Val Thr Arg His Ala Asp Val Ile Pro Val Arg Arg Arg		
	325	330	335

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Gly Asp Ser Arg Gly Ser Leu Leu Ser Pro Arg Pro Val Ser Tyr Leu
 340 345 350

5 Lys Gly Ser Ser Gly Gly Pro Leu Leu Cys Pro Phe Gly His Ala Val
 355 360 365

Gly Ile Phe Arg Ala Ala Val Cys Thr Arg Gly Val Ala Lys Ala Val
 370 375 380

Asp Phe Val Pro Val Glu Ser Met Glu Thr Thr Met Arg Ser Pro Val
 385 390 395 400

10 Phe Thr Asp Asn Ser Ser Pro Pro Ala Val Pro Gln Ser Phe Gln Val
 405 410 415

Ala His Leu His Ala Pro Thr Gly Ser Gly Lys Ser Thr Lys Val Pro
 420 425 430

15 Ala Ala Tyr Ala Ala Gln Gly Tyr Lys Val Leu Val Leu Asn Pro Ser
 435 440 445

Val Ala Ala Thr Leu Gly Phe Gly Ala Tyr Met Ser Lys Ala His Gly
 450 455 460

Ile Asp Pro Asn Ile Arg Thr Gly Val Arg Thr Ile Thr Thr Gly Ala
 465 470 475 480

20 Pro Val Thr Tyr Ser Thr Tyr Gly Lys Phe Leu Ala Asp Gly Gly Cys
 485 490 495

Ser Gly Gly Ala Tyr Asp Ile Ile Ile Cys Asp Glu Cys His Ser Thr
 500 505 510

25 Asp Ser Thr Thr Ile Leu Gly Ile Gly Thr Val Leu Asp Gln Ala Glu
 515 520 525

Thr Ala Gly Ala Arg Leu Val Val Leu Ala Thr Ala Thr Pro Pro Gly
 530 535 540

Ser Val Thr Val Pro His Pro Asn Ile Glu Glu Val Ala Leu Ser Asn
 545 550 555 560

30 Thr Gly Glu Ile Pro Phe Tyr Gly Lys Ala Ile Pro Ile Glu Ala Ile
 565 570 575

Arg Gly Gly Arg His Leu Ile Phe Cys His Ser Lys Lys Lys Cys Asp
 580 585 590

35 Glu Leu Ala Ala Lys Leu Ser Gly Leu Gly Ile Asn Ala Val Ala Tyr
 595 600 605

Tyr Arg Gly Leu Asp Val Ser Val Ile Pro Thr Ile Gly Asp Val Val
 610 615 620

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	Val Val Ala Thr Asp Ala Leu Met Thr Gly Tyr Thr Gly Asp Phe Asp	
	625	630 635 640
5	Ser Val Ile Asp Cys Asn Thr Cys Val Thr Gln Thr Val Asp Phe Ser	
	645	650 655
	Leu Asp Pro Thr Phe Thr Ile Glu Thr Thr Thr Val Pro Gln Asp Ala	
	660	665 670
	Val Ser Arg Ser Gln Arg Arg Gly Arg Thr Gly Arg Gly Arg Arg Gly	
	675	680 685
10	Ile Tyr Arg Phe Val Thr Pro Gly Glu Arg Pro Ser Gly Met Phe Asp	
	690	695 700
	Ser Ser Val Leu Cys Glu Cys Tyr Asp Ala Gly Cys Ala Trp Tyr Glu	
	705	710 715 720
	Leu Thr Pro Ala Glu Thr Ser Val Arg Leu Arg Ala Tyr Leu Asn Thr	
15	725	730 735
	Pro Gly Leu Pro Val Cys Gln Asp His Leu Glu Phe Trp Glu Ser Val	
	740	745 750
	Phe Thr Gly Leu Thr His Ile Asp Ala His Phe Leu Ser Gln Thr Lys	
	755	760 765
20	Gln Ala Gly Asp Asn Phe Pro Tyr Leu Val Ala Tyr Gln Ala Thr Val	
	770	775 780
	Cys Ala Arg Ala Gln Ala Pro Pro Pro Ser Trp Asp Gln Met Trp Lys	
	785	790 795 800
	Cys Leu Ile Arg Leu Lys Pro Thr Leu His Gly Pro Thr Pro Leu Leu	
25	805	810 815
	Tyr Arg Leu Gly Ala Val Gln Asn Glu Val Thr Leu Thr His Pro Ile	
	820	825 830
	Thr Lys Tyr Ile Met Ala Cys Met Ser Ala Asp Leu Glu Val Val Thr	
	835	840 845
30	Ser Thr Trp Val Leu Val Gly Gly Val Leu Ala Ala Leu Ala Ala Tyr	
	850	855 860
	Cys Leu Thr Thr Gly Ser Val Val Ile Val Gly Arg Ile Ile Leu Ser	
	865	870 875 880
	Gly Arg Pro Ala Ile Val Pro Asp Arg Glu Leu Leu Tyr Gln Glu Phe	
35	885	890 895
	Asp Glu Met Glu Glu Cys Ala Ser His Leu Pro Tyr Ile Glu Gln Gly	
	900	905 910

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Ser Cys Gln Arg Gly Tyr Lys Gly Val Trp Arg Gly Asp Gly Ile Met
1205 1210 1215

Gln Thr Thr Cys Pro Cys Gly Ala Gln Ile Thr Gly His Val Lys Asn
5 1220 1225 1230

Gly Ser Met Arg Ile Val Gly Pro Lys Thr Cys Ser Asn Thr Trp His
1235 1240 1245

Gly Thr Phe Pro Ile Asn Ala Tyr Thr Thr Gly Pro Cys Thr Pro Ser
1250 1255 1260

10 Pro Ala Pro Asn Tyr Ser Arg Ala Leu Trp Arg Val Ala Ala Glu Glu
1265 1270 1275 1280

Tyr Val Glu Val Thr Arg Val Gly Asp Phe His Tyr Val Thr Gly Met
1285 1290 1295

Thr Thr Asp Asn Val Lys Cys Pro Cys Gln Val Pro Ala Pro Glu Phe
15 1300 1305 1310

Phe Ser Glu Val Asp Gly Val Arg Leu His Arg Tyr Ala Pro Ala Cys
1315 1320 1325

Arg Pro Leu Leu Arg Glu Glu Val Thr Phe Gln Val Gly Leu Asn Gln
1330 1335 1340

20 Tyr Leu Val Gly Ser Gln Leu Pro Cys Glu Pro Glu Pro Asp Val Ala
1345 1350 1355 1360

Val Leu Thr Ser Met Leu Thr Asp Pro Ser His Ile Thr Ala Glu Thr
1365 1370 1375

Ala Lys Arg Arg Leu Ala Arg Gly Ser Pro Pro Ser Leu Ala Ser Ser
25 1380 1385 1390

Ser Ala Ser Gln Leu Ser Ala Pro Ser Leu Lys Ala Thr Cys Thr Thr
1395 1400 1405

His His Val Ser Pro Asp Ala Asp Leu Ile Glu Ala Asn Leu Leu Trp
1410 1415 1420

30 Arg Gln Glu Met Gly Gly Asn Ile Thr Arg Val Glu Ser Glu Asn Lys
1425 1430 1435 1440

Val Val Val Leu Asp Ser Phe Asp Pro Leu Arg Ala Glu Glu Asp Glu
1445 1450 1455

Arg Glu Val Ser Val Pro Ala Glu Ile Leu Arg Lys Ser Lys Lys Phe
35 1460 1465 1470

Pro Ala Ala Met Pro Ile Trp Ala Arg Pro Asp Tyr Asn Pro Pro Leu
1475 1480 1485

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Leu Glu Ser Trp Lys Asp Pro Asp Tyr Val Pro Pro Val Val His Gly
 1490 1495 1500

5 Cys Pro Leu Pro Pro Ile Lys Ala Pro Pro Ile Pro Pro Pro Arg Arg
 1505 1510 1515 1520
 Lys Arg Thr Val Val Leu Thr Glu Ser Ser Val Ser Ser Ala Leu Ala
 1525 1530 1535
 Glu Leu Ala Thr Lys Thr Phe Gly Ser Ser Glu Ser Ser Ala Val Asp
 1540 1545 1550

10 Ser Gly Thr Ala Thr Ala Leu Pro Asp Gln Ala Ser Asp Asp Gly Asp
 1555 1560 1565
 Lys Gly Ser Asp Val Glu Ser Tyr Ser Ser Met Pro Pro Leu Glu Gly
 1570 1575 1580
 Glu Pro Gly Asp Pro Asp Leu Ser Asp Gly Ser Trp Ser Thr Val Ser
 1585 1590 1595 1600
 Glu Glu Ala Ser Glu Asp Val Val Cys Cys Ser Met Ser Tyr Thr Trp
 1605 1610 1615
 Thr Gly Ala Leu Ile Thr Pro Cys Ala Ala Glu Glu Ser Lys Leu Pro
 1620 1625 1630

20 Ile Asn Ala Leu Ser Asn Ser Leu Leu Arg His His Asn Met Val Tyr
 1635 1640 1645
 Ala Thr Thr Ser Arg Ser Ala Gly Leu Arg Gln Lys Lys Val Thr Phe
 1650 1655 1660
 Asp Arg Leu Gln Val Leu Asp Asp His Tyr Arg Asp Val Leu Lys Glu
 1665 1670 1675 1680
 Met Lys Ala Lys Ala Ser Thr Val Lys Ala Lys Leu Leu Ser Val Glu
 1685 1690 1695
 Glu Ala Cys Lys Leu Thr Pro Pro His Ser Ala Lys Ser Lys Phe Gly
 1700 1705 1710

30 Tyr Gly Ala Lys Asp Val Arg Asn Leu Ser Ser Lys Ala Val Asn His
 1715 1720 1725
 Ile His Ser Val Trp Lys Asp Leu Leu Glu Asp Thr Val Thr Pro Ile
 1730 1735 1740
 Asp Thr Thr Ile Met Ala Lys Asn Glu Val Phe Cys Val Gln Pro Glu
 1745 1750 1755 1760
 Lys Gly Gly Arg Lys Pro Ala Arg Leu Ile Val Phe Pro Asp Leu Gly
 1765 1770 1775

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Val Arg Val Cys Glu Lys Met Ala Leu Tyr Asp Val Val Ser Thr Leu
 1780 1785 1790

5 Pro Gln Val Val Met Gly Ser Ser Tyr Gly Phe Gln Tyr Ser Pro Gly
 1795 1800 1805

Gln Arg Val Glu Phe Leu Val Asn Thr Trp Lys Ser Lys Lys Asn Pro
 1810 1815 1820

Met Gly Phe Ser Tyr Asp Thr Arg Cys Phe Asp Ser Thr Val Thr Glu
 1825 1830 1835 1840

10 Asn Asp Ile Arg Val Glu Glu Ser Ile Tyr Gln Cys Cys Asp Leu Ala
 1845 1850 1855

Pro Glu Ala Arg Gln Ala Ile Lys Ser Leu Thr Glu Arg Leu Tyr Ile
 1860 1865 1870

Gly Gly Pro Leu Thr Asn Ser Lys Gly Gln Asn Cys Gly Tyr Arg Arg
 1875 1880 1885

15 Cys Arg Ala Ser Gly Val Leu Thr Thr Ser Cys Gly Asn Thr Leu Thr
 1890 1895 1900

Cys Tyr Leu Lys Ala Ser Ala Ala Cys Arg Ala Ala Lys Leu Gln Asp
 1905 1910 1915 1920

20 Cys Thr Met Leu Val Asn Gly Asp Asp Leu Val Val Ile Cys Glu Ser
 1925 1930 1935

Ala Gly Thr Gln Glu Asp Ala Ala Ser Leu Arg Val Phe Thr Glu Ala
 1940 1945 1950

Met Thr Arg Tyr Ser Ala Pro Pro Gly Asp Pro Pro Gln Pro Glu Tyr
 1955 1960 1965

25 Asp Leu Glu Leu Ile Thr Ser Cys Ser Ser Asn Val Ser Val Ala His
 1970 1975 1980

Asp Ala Ser Gly Lys Arg Val Tyr Tyr Leu Thr Arg Asp Pro Thr Thr
 1985 1990 1995 2000

30 Pro Leu Ala Arg Ala Ala Trp Glu Thr Ala Arg His Thr Pro Val Asn
 2005 2010 2015

Ser Trp Leu Gly Asn Ile Ile Met Tyr Ala Pro Thr Leu Trp Ala Arg
 2020 2025 2030

Met Ile Leu Met Thr His Phe Phe Ser Ile Leu Leu Ala Gln Glu Gln
 2035 2040 2045

35 Leu Glu Lys Ala Leu Asp Cys Gln Ile Tyr Gly Ala Cys Tyr Ser Ile
 2050 2055 2060

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Ala Phe Ser Leu His Ser Tyr Ser Pro Gly Glu Ile Asn Arg Val Ala	2085	2090	2095
Ser Cys Leu Arg Lys Leu Gly Val Pro Pro Leu Arg Val Trp Arg His	2100	2105	2110
Arg Ala Arg Ser Val Arg Ala Arg Leu Leu Ser Gln Gly Gly Arg Ala	2115	2120	2125
Ala Thr Cys Gly Lys Tyr Leu Phe Asn Trp Ala Val Lys Thr Lys Leu	2130	2135	2140
Lys Leu Thr Pro Ile Pro Ala Ala Ser Arg Leu Asp Leu Ser Gly Trp	2145	2150	2155
Phe Val Ala Gly Tyr Ser Gly Gly Asp Ile Tyr His Ser Leu Ser Arg	2160	2165	2170
Ala Arg Pro Arg Trp Phe Met Leu Cys Leu Leu Leu Leu Ser Val Gly	2175	2180	2185
Val Gly Ile Tyr Leu Leu Pro Asn Arg	2190	2195	2200

(3) INFORMATION FOR SEQ ID NO: 3

- (i) SEQUENCE CHARACTERISTICS
 - (A) LENGTH: 26 nucleotides
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: synthetic DNA
- (iii) HYPOTHETICAL: No
- (iv) ANTISENSE: No
- (vii) IMMEDIATE SOURCE: oligonucleotide synthesizer
- (ix) FEATURE:
 - (A) NAME: oligo a
 - (C) IDENTIFICATION METHOD: Polyacrylamide gel
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3

GCCGAGATGC CATCTTCAAA CAGTTC

26

(4) INFORMATION FOR SEQ ID NO: 4

(i) SEQUENCE CHARACTERISTICS

- 5 (A) LENGTH: 24 nucleotides
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: synthetic DNA

(iii) HYPOTHETICAL: No

(iv) ANTISENSE: No

(vii) IMMEDIATE SOURCE: oligonucleotide
synthesizer

(ix) FEATURE:

15 (A) NAME: oligo b

(C) IDENTIFICATION METHOD: Polyacrylamide
gel

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4

20 GTGTACAACA AGGTCCATAT CACC

24

(5) INFORMATION FOR SEQ ID NO: 5

(i) SEQUENCE CHARACTERISTICS

- 25 (A) LENGTH: 24 nucleotides
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: synthetic DNA

(iii) HYPOTHETICAL: No

30 (iv) ANTISENSE: No

(vii) IMMEDIATE SOURCE: oligonucleotide
synthesizer

(ix) FEATURE:

35 (A) NAME: oligo c

(C) IDENTIFICATION METHOD: Polyacrylamide
gel

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5

GGTCTTTCTG AACGGGATAT AAAC

24

(6) INFORMATION FOR SEQ ID NO: 6:

5 (i) SEQUENCE CHARACTERISTICS
(A) LENGTH: 31 nucleotides
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

10 (ii) MOLECULE TYPE: synthetic DNA
(iii) HYPOTHETICAL: No
(iv) ANTISENSE: No
(vii) IMMEDIATE SOURCE: oligonucleotide
synthesizer

15 (ix) FEATURE:
(A) NAME: 5'-5B
(C) IDENTIFICATION METHOD: Polyacrylamide
gel

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 6

AAGGATCCAT GTCAATGTCC TACACATGGA C 31

(7) INFORMATION FOR SEQ ID NO: 7:

25 (i) SEQUENCE CHARACTERISTICS
(A) LENGTH: 36 nucleotides
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

30 (ii) MOLECULE TYPE: synthetic DNA
(iii) HYPOTHETICAL: No
(iv) ANTISENSE: Yes
(vii) IMMEDIATE SOURCE: oligonucleotide
synthesizer

35 (ix) FEATURE:
(A) NAME: 3'-5B
(C) IDENTIFICATION METHOD: Polyacrylamide
gel

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 7

AATATTGAA TTCATCGGTT GGGGAGCAGG TAGATG

36

5 (8) INFORMATION FOR SEQ ID NO: 8:

(i) SEQUENCE CHARACTERISTICS
(A) LENGTH: 22 nucleotides

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: synthetic DNA

(iii) HYPOTHETICAL: No

(iv) ANTISENSE: No

(vii) IMMEDIATE SOURCE: oligonucleotide
synthesizer

(ix) FEATURE:

(A) NAME: Dpr1

(C) IDENTIFICATION METHOD: Polyacrylamide
gel

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 8

TGGCTGGCAA GGCACACAGG CT

22

25 (9) INFORMATION FOR SEQ ID NO: 9

(i) SEQUENCE CHARACTERISTICS
(A) LENGTH: 20 nucleotides

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

30 (ii) MOLECULE TYPE: synthetic DNA

(iii) HYPOTHETICAL: No

(iv) ANTISENSE: Yes

(vii) IMMEDIATE SOURCE: oligonucleotide
synthesizer

35 (ix) FEATURE:

(A) NAME: Dpr2

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(C) IDENTIFICATION METHOD: Polyacrylamide
gel

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 9

5 AGGCAGGGTA GATCTATGTC 20

(10) INFORMATION FOR SEQ ID NO: 10

(i) SEQUENCE CHARACTERISTICS

(A) LENGTH: 20 nucleotides

10 (B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: synthetic DNA

(iii) HYPOTHETICAL: No

15 (iv) ANTISENSE: No

(vii) IMMEDIATE SOURCE: oligonucleotide
synthesizer

(ix) FEATURE:

(A) NAME: NS5B-5' (1)

20 (C) IDENTIFICATION METHOD: Polyacrylamide
gel

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 10

TCAATGTCCT ACACATGGAC 20

25

(11) INFORMATION FOR SEQ ID NO: 11

(i) SEQUENCE CHARACTERISTICS

(A) LENGTH: 38 nucleotides

(B) TYPE: nucleic acid

30 (C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: synthetic DNA

(iii) HYPOTHETICAL: No

(iv) ANTISENSE: Yes

35 (vii) IMMEDIATE SOURCE: oligonucleotide
synthesizer

(ix) FEATURE:

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(A) NAME: HCVA-13

(C) IDENTIFICATION METHOD: Polyacrylamide
gel

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 11

5

GATCTCTAGA TCATCGGTTG GGGGAGGAGG TAGATGCC

38

(12) INFORMATION FOR SEQ ID NO: 12

(i) SEQUENCE CHARACTERISTICS

10

(A) LENGTH: 399 nucleotides

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: mRNA

15

(iii) HYPOTHETICAL: No

(iv) ANTISENSE: No

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Rattus Norvegicus

(B) STRAIN : Sprague-Dawley

20

(vii) IMMEDIATE SOURCE: pT7-7 (DCoH)

(ix) FEATURE:

(A) NAME: D-RNA

(C) IDENTIFICATION METHOD: Polyacrylamide
gel

25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 12

GGGAGACCAC AACGGUUUCC CUCUAGAAAU AAUUUUGUUU AACUUUAAGA AGGAGAUAVA 60

CAUAUGGCUA GAAUUCGCGC CCUGGCUGGC AAGGCACACA GGCUGAGUGC UGAGGAACGG 120

GACCAGCUGC UGCCAAACCU GCGGGCCGUG GGGUGGAUG AACUGGAAGG CCGAGAUGCC 180

30 AUUUCAAAC AGUCCAUUU UAAAGACUUC AACAGGGCUU UUGGCUUCAU GACAAGAGUC 240

GCCCUGCAGG CUGAAAAGCU GGACCACCAU CCCGAGUGGU UUAACGUGUA CAACAAGGUC 300

CAUAUCACCU UGAGCACCCA CGAUGUGCC GGUCUUUCUG AACGGGAUUA AAACCUGGCC 360

AGCUUCAUCG AACAAGUUGC CGUGUCUAUG ACAUAGAUC 399

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(13) INFORMATION FOR SEQ ID NO: 13:

(i) SEQUENCE CHARACTERISTICS

- 5 (A) LENGTH: 20 nucleotides
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: synthetic DNA
(iii) HYPOTHETICAL: No
(iv) ANTISENSE: No
10 (vii) IMMEDIATE SOURCE: oligonucleotide synthesizer
(ix) FEATURE:
(A) NAME: NS5B-up
(C) IDENTIFICATION METHOD: Polyacrylamide gel
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 13

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TGTC AATGTC CTACACATGG

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(14) INFORMATION FOR SEQ ID NO: 14:

(i) SEQUENCE CHARACTERISTICS

- 20 (A) LENGTH: 38 nucleotides
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: synthetic DNA
25 (iii) HYPOTHETICAL: No
(iv) ANTISENSE: Yes
(vii) IMMEDIATE SOURCE: oligonucleotide synthesizer
(ix) FEATURE:
(A) NAME: 3'-5B
30 (C) IDENTIFICATION METHOD: Polyacrylamide gel
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 14

AATATTCGAA TTCATCGGTT GGGGAGCAGG TAGATG

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